

AMENDMENTS TO THE SPECIFICATION

Please replace the sequence listing submitted on November 14, 2007 with the amended sequence listing provided herewith.

Please insert the following paragraphs at page 1, line 10 of the substitute specification filed on November 16, 2005:

REFERENCE TO A SEQUENCE LISTING APPENDIX

A Sequence Listing is provided in this patent document as a .txt file entitled, "50538_016001_ST25.txt," created September 23, 2009 (size: 2.52 KB).

The content of this file is herein incorporated by reference.

Please replace the paragraphs beginning at page 2, line 16 of the substitute specification filed on November 16, 2005 with the following replacement paragraphs:

MBPCs for use in the treatment of HIV infections were first described by J-M. Sabatier et al in WO 95/07929. The MBPCs described therein have peptides which contain the sequence GPGR (**SEQ ID NO: 1**) (from the V3 loop of the surface envelope glycoprotein gp120 of HIV) preceded by from 0 to 4 amino acid residues and succeeded by from 2 to 4 amino acid residues. The amino acid sequences IGPGR (**SEQ ID NO: 2**) and IXXGPGR (**SEQ ID NO: 3**) (where X is an amino acid residue) are excluded. The most preferred of these MBPCs has a lysine residue core with eight peptides GPGRA (**SEQ ID NO: 4**) bonded thereto. It may be represented as (GPGRA (**SEQ ID NO: 4**))₈-K₄-K₂-K-βA-OH (**SEQ ID NO: 5**), the OH terminal indicating the carboxyl group of the β-alanine. That carboxyl group may alternatively be modified to form a carboxamide terminal. This compound is referred to herein as SPC3.

In WO 98/29443, J-M Sabatier et al described further MBPCs which may be effective in the treatment of HIV infection. These use peptides derived from the HIV envelope transmembrane glycoprotein gp41. The peptides contain the sequence RQGY (**SEQ ID NO: 6**) preceded by from 0

to 4 amino acid residues and succeeded by from 2 to 4 amino acid residues. The most preferred of these MBPCs has a lysine residue core with eight peptides RQGYSPL (SEQ ID NO: 7) bonded thereto. It may be represented as (RQGYSPL (SEQ ID NO: 7))₈-K₄-K₂-K-βA-OH (SEQ ID NO: 5), the OH terminal indicating the carboxyl group of the β-alanine. That carboxyl group may alternatively be modified to form a carboxamide terminal. This compound is referred to herein as RL, although it has in the past also been referred to as SPC RL and as RL41.

Subsequently to WO 98/29443, it was established that the MBPC (RQGYSPL (SEQ ID NO: 7))₂-K-βA (hereinafter RL dimer) is effective but that the MBPC (RQGYSP (SEQ ID NO: 8))₂-K-βA is less so. This was thought to confirm the lower limit of 6 amino acids in the peptide branches of the MBPCs. However, K Mabrouk et al showed in WO 03/095479 that some shorter peptides could be used, in particular (RQGYS (SEQ ID NO: 9))₂-K-βA-OH (hereinafter RS, but in the past also referred to as Short RL) and (RQGY (SEQ ID NO: 6))₈-K₄-K₂-K-βA-OH (SEQ ID NO: 5).

SPC3 and RL both have 8 branches and are described as octomers. RS has two branches, and is described as a dimer. None of the monomers, that is the linear peptides GPGRAf (SEQ ID NO: 4), RQGYSPL (SEQ ID NO: 7) and RQGY (SEQ ID NO: 9), has ever shown any activity.

Please replace the paragraphs beginning at page 4, line 6 of the substitute specification filed on November 16, 2005 with the following replacement paragraphs:

The invention provides a compound comprising a water soluble antiviral peptide including one of the sequences GPG and RQGY (SEQ ID NO: 6) and, bonded to the C-end of the peptide, a terminator which is either (a) an ω-amino-fatty acid having from 4 to 10 carbon atoms and from 0 to 2 carbon-carbon double bonds or (b) a peptidic cell membrane penetrating agent.

The antiviral peptide may be an MBPC with a lysine core matrix. In such a case the terminator is bonded to the root lysine residue. The MBPCs described above may be used, that is to say SPC3 which has 8 branches of GPGRAf (SEQ ID NO: 4), RL which has 8 branches of RQGYSPL (SEQ ID NO: 7) and RS which has 2 branches of RQGY (SEQ ID NO: 9). However, the improvement resulting from the bonding of the terminator to

the C-end of the antiviral peptide is so great that SPC3 and RL can be reduced to two branches (SPC3 dimer and RL dimer, respectively), or even to one branch (SPC3 monomer and RL monomer, respectively), while RS may also be reduced to one branch (RS monomer). Further work has even indicated that SPC3 monomer (GPGRAF) **(SEQ ID NO: 4)** may be shortened to GRGRA **(SEQ ID NO: 10)**, GPGR **(SEQ ID NO: 1)** or GPC. As these are much smaller molecules, they are much easier and cheaper to make and are preferred for that reason.

Please replace the paragraph beginning at page 5, line 16 of the substitute specification filed on November 16, 2005 with the following replacement paragraph:

We also synthesized shortened peptides related to SPC3 monomer, which is GPGRAF (**SEQ ID NO: 4**), in particular GRGRA (**SEQ ID NO: 10**), GPGR (**SEQ ID NO: 1**) and GPG and tested these with a δ -aminovaleric acid terminator. These were tested twice, 8 days apart, on C8166 cells against HIV-1 NL 4-3 (results are shown in Tables 6 and 7) and on C8166 cells against HIV-1 NDK (results are shown in Table 8).

Please replace Table 3, found at page 11, line 1 of the substitute specification filed on November 16, 2005 with the following replacement table:

Table 3

Antiviral Activity Experiment on C8166 cells with HIV-1 subtype B NL 4-3

Name	Formula	IC ₅₀ (μ M)
SPC3	(GPGRAF (SEQ ID NO: 4)) ₈ -K ₄ -K ₂ -K-NHCH ₂ CH ₂ COOH (SEQ ID NO: 5)	0.5
SPC3 dimer valeric acid	(GPGRAF (SEQ ID NO: 4)) ₂ -K-NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.05
SPC3 monomer	GPGRAF (SEQ ID NO: 4)	>10
SPC3 monomer valeric acid	GPGRAF (SEQ ID NO: 4)-NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.02
RL	(RQGYSPL (SEQ ID NO: 7)) ₈ -K ₄ -K ₂ -K-NHCH ₂ CH ₂ COOH (SEQ ID NO: 5)	0.01
RL dimer	(RQGYSPL (SEQ ID NO: 7)) ₂ -K-NHCH ₂ CH ₂ COOH	0.02
RL monomer	RQGYSPL (SEQ ID NO: 7)	0.5
RL dimer valeric acid	(RQGYSPL (SEQ ID NO: 7)) ₂ -K-NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.05
RL monomer valeric acid	RQGYSPL (SEQ ID NO: 7)-NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.05
RS	(RQGYS (SEQ ID NO: 9)) ₂ -K-NHCH ₂ CH ₂ COOH	0.1
RS monomer	RQGYS (SEQ ID NO: 9)	0.2

RS dimer valeric acid	(RQGYYS (SEQ ID NO: 9)) ₂ -K-NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.05
RS monomer valeric acid	RQGYYS (SEQ ID NO: 9)-NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.2

Please replace Table 4, found at page 11 of the substitute specification filed on November 16, 2005 with the following replacement table:

Table 4

Experiment on PBL with NL 4-3 strain

Name	Formula	IC ₅₀ (μM)	IC ₁₀₀ (μM)
SPC3	(GPGRAP (SEQ ID NO: 4)) ₈ -K ₄ -K ₂ -K-NHCH ₂ CH ₂ COOH (SEQ ID NO: 5)	0.01	0.1
SPC3 monomer valeric acid	GPGRAP (SEQ ID NO: 4)-NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.02	0.1
RL	(RQGYSP (SEQ ID NO: 7)) ₈ -K ₄ -K ₂ -K-NHCH ₂ CH ₂ COOH (SEQ ID NO: 5)	0.005	0.1
RL dimer	(RQGYSP (SEQ ID NO: 7)) ₂ -K-NHCH ₂ CH ₂ COOH	0.01	0.1
RL dimer valeric acid	(RQGYSP (SEQ ID NO: 7)) ₂ -K-NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.005	0.05
RL monomer valeric acid	RQGYSP (SEQ ID NO: 7)-NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.01	1

Please replace Table 5, found at page 12, line 1 of the substitute specification filed on November 16, 2005 with the following replacement table.

Table 5

Experiment on PBMC with HIV-1 89.6 subtype B dualtropic (X4R5)

Name	Formula	IC ₅₀ (μM)	IC ₁₀₀ (μM)
SPC3	(GPGRAF (SEQ ID NO: 4)) ₈ -K ₄ -K ₂ -K-NHCH ₂ CH ₂ COOH (SEQ ID NO: 5)	0.06	0.5
SPC3 dimer valeric acid	(GPGRAF (SEQ ID NO: 4)) ₂ -K-NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.008	0.5
SPC3 monomer valeric acid	GPGRAF (SEQ ID NO: 4) -NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.01	0.5
RL	(RQGYSP (SEQ ID NO: 7)) ₈ -K ₄ -K ₂ -K-NHCH ₂ CH ₂ COOH (SEQ ID NO: 5)	0.006	0.05
RL dimer valeric acid	(RQGYSP (SEQ ID NO: 7)) ₂ -K-NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.01	0.5
RL monomer valeric acid	RQGYSP (SEQ ID NO: 7) -NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.01	0.1

Please replace Table 6, found at page 11 of the substitute specification filed on November 16, 2005 with the following replacement table:

Table 6

Antiviral Activity Experiment on C8166 cells with HIV NL-4-3

GPG	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 μM	-		-	-	-	1
	-		-	-	-	5
1 μM	-		-	-	-	3.8
	-		-	-	-	5.4

0.5 μ M	-		-	-	-	7.9
	-		-	-	-	18
0.1 μ M	-		-	-	+	525
	-		-	-	+	5764
0.05 μ M	-		-	(+)	+	7330
	-		-	(+)	+	9810
0.01 μ M	-		(+)	+	++	13850
	-		(+)	+	++	11756
0.005 μ M	-		+	++	++/T	23810
	-		+	++	++/T	23810
GPG valeric acid	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 μ M	-		-	-	-	5.6
	-		-	-	-	3.2
1 μ M	-		-	-	-	5.636
	-		-	-	-	4.8
0.5 μ M	-		-	-	-	3.5
	-		-	-	-	5.6
0.1 μ M	-		-	(+)	+	126
	-		-	(+)	+	3810
0.05 μ M	-		-	(+)	+	1850
	-		-	(+)	+	9867
0.01 μ M	-		+	+	++	11810
	-		+	+	++	13740
0.005 μ M	-		+	++	++/T	23810
	-		+	++	++/T	23810
GPGR (SEQ ID NO: 1)	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 μ M	-		-	-	-	9.425
	-		-	-	-	3.375
1 μ M	-		-	-	+	1103
	-		-	-	+	485
0.5 μ M	-		-	-	+	2507
	-		-	-	+	2840
0.1 μ M	-		(+)	+	+	5810
	-		(+)	+	+	10110
0.05 μ M	-		+	+	++	2507
	-		+	+	++	13870
0.01 μ M	-		+	++	++	23810
	-		+	++	++	23810
0.005 μ M	-		++	++	++/T	23810
	-		++	++	++/T	23810
GPGR (SEQ ID NO: 1) valeric acid	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 μ M	-		-	-	-	2.36
	-		-	-	-	2.4
1 μ M	-		-	-	+	104
	-		-	-	+	179
0.5 μ M	-		-	-	+	105
	-		-	-	+	510
0.1 μ M	-		(+)	+	+	433
	-		(+)	+	+	507
0.05 μ M	-		(+)	+	++	9840
	-		(+)	+	++	11830
0.01 μ M	-		+	++	++	21800
	-		+	++	++	23810

0.005µM	-		+	++	++	23810
	-		+	++	++	23810
GPGRA (SEQ ID NO: 11)	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 µM	-		-	-	-	3.62
	-		-	-	-	13
1 µM	-		-	-	-	2.9
	-		-	-	-	3.2
0.5 µM	-		-	-	-	2.1
	-		-	-	-	2.1
0.1µM	-		(+)	+	+	2838
	-		(+)	+	+	2435
0.05µM	-		(+)	+	++	4230
	-		(+)	+	++	8910
0.01µM	-		+	++	++/T	15650
	-		+	++	++/T	16810
0.005µM	-		+	++	++/T	23810
	-		+	++	++/T	23810
GPGRA (SEQ ID NO: 11) valeric acid	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 µM	-		-	-	-	2.7
	-		-	-	-	1.8
1 µM	-		-	-	-	2.3
	-		-	-	-	1.9
0.5 µM	-		-	-	-	2
	-		-	-	-	2.2
0.1µM	-		(+)	+	+	2352
	-		(+)	+	+	1011
0.05µM	-		(+)	+	+	6830
	-		(+)	+	+	3820
0.01µM	-		+	++	++	13030
	-		+	++	++	13810
0.005µM	-		+	++	++/T	23810
	-		+	++	++/T	23810
SPC3 (SEQ ID NO: 4) monomer valeric acid	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 µM	-		-	-	-	3
	-		-	-	-	3
1 µM	-		-	-	(+)	325
	-		-	-	(+)	445
0.5 µM	-		-	(+)	+	1840
	-		-	(+)	+	2830
0.1µM	-		(+)	+	++	11810
	-		(+)	++	++	1507
0.05µM	-		+	++	++	3810
	-		+	++	++	21810
0.01µM	-		+	++	++/T	21810
	-		+	++	++/T	21810
0.005µM	-		+	++	++/T	23810
	-		+	++	++/T	23810
SPC3	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 µM	-		-	-	-	3
	-		-	-	-	3
1 µM	-		-	-	(+)	1692
	-		-	-	(+)	776

0.5 µM	-		-	(+)	+	5173
	-		-	(+)	+	4840
0.1µM	-		(+)	+	++	17810
	-		(+)	++	++	19850
0.05µM	-		+	++	++ /T	23810
	-		+	++	++/T	23810
0.01µM	-		+	++	++ /T	23810
	-		+	++	++/T	23810
0.005µM	-		+	++	++ /T	23810
	-		+	++	++/T	23810

T Cell	-		-	-	-	3
	-		-	-	-	3
L4-3 1/1000	(+)		+	++	++ /T	23810
	(+)		+	++	++/T	23810

Please replace Table 7, found at page 14 of the substitute specification filed on November 16, 2005 with the following replacement table:

Table 7

Antiviral Activity Experiment on C8166 cells with HIV NL-4-3

GPG	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 µM	-		-	-	-	2
	-		-	-	-	79
1 µM	-		-	-	(+)	42
	-		-	-	(+)	62
0.5 µM	-		-	-	(+)	126
	-		-	-	(+)	165
0.1µM	-		-	(+)	+	807
	-		-	(+)	+	1506
0.5µM	-		-	(+)	+	1810
	-		-	(+)	+	3810
0.01µM	(+)		(+)	+	++	9810
	(+)		(+)	+	++	15810
GPG valeric acid	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 µM	-		-	-	-	60
	-		-	-	-	34
1 µM	-		-	-	-	86
	-		-	-	-	74
0.5 µM	-		-	-	(+)	126
	-		-	-	(+)	44
0.1µM	-		-	(+)	+	108
	-		-	(+)	+	130
0.05µM	-		-	(+)	+	3810
	-		-	(+)	+	2300

0.01µM	-		(+)	+	++	3800
	-		(+)	+	++	23000
GPGR (SEQ ID NO: 1)	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 µM	-		-	-	(+)	152
	-		-	-	(+)	152
1 µM	-		-	-	(+)	316
	-		-	-	(+)	343
0.5 µM	-		-	-	+	23000
	-		-	-	+	15810
0.1µM	-		(+)	+	+	5810
	-		(+)	+	+	23000
0.05µM	(+)		+	+	++	13810
	(+)		+	+	++	12980
0.01µM	(+)		+	++	++	23810
	(+)		+	++	++	23810
GPGR (SEQ ID NO: 1) valeric acid	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 µM	-		-	-	-	2
	-		-	-	-	2
1 µM	-		-	-	-	53
	-		-	-	-	64
0.5 µM	-		-	-	+	2740
	-		-	-	+	2840
0.1µM	-		(+)	+	+	2173
	-		(+)	+	+	9810
0.05µM	-		(+)	+	++	9860
	-		(+)	+	++	17800
0.01µM	-		+	++	++/T	3800
	-		+	++	++	21300
GPGRA (SEQ ID NO: 11)	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 µM	-		-	-	(+)	99
	-		-	-	(+)	100
1 µM	-		-	-	(+)	117
	-		-	-	(+)	119
0.5 µM	-		-	-	+	2070
	-		-	-	+	5410
0.1µM	-		(+)	+	+	2837
	-		(+)	+	++	9310
0.05µM	-		(+)	+	++	4230
	-		(+)	+	++	8910
0.01µM	-		+	++	++/T	15650
	-		+	++	++/T	16810
GPGRA (SEQ ID NO: 11) valeric acid	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 µM	-		-	-	-	2.7
	-		-	-	-	3
1 µM	-		-	-	-	13
	-		-	-	-	10
0.5 µM	-		-	-	(+)	234
	-		-	-	(+)	576
0.1µM	-		-	(+)	+	2356
	-		-	(+)	+	2416

0.05μM	-		(+)	+	+	3810
	-		(+)	+	+	11820
0.01μM	-		+	++	++	13870
	-		+	++	++	11810
T Cell	-		-	-	-	2
	-		-	-	-	6
L4-3 1/1000	(+)		+	++	++ /T	23810
	(+)		+	++	++/T	15670
					++ /T	19750

Please replace Table 8 found at page 16 of the substitute specification filed on November 16, 2005 with the following replacement table:

Table 8

Antiviral Activity Experiment on C8166 cells with HIV 1 NDK

GPG	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 μM	-		-	-	+	2733
	-		-	-	+	2400
1 μM	-		(+)	+	+	2507
	-		(+)	+	+	3810
0.5 μM	-		+	++	++	21110
	-		+	++	++	23810
0.1μM	-		+	++	++	23810
	-		+	++	++	23810
0.05μM	(+)		+	++	++	23810
	(+)		+	++	++	23810
0.01μM	+		+	++	++	23810
	+		+	++	++	23810
0.005μM	+		+	++	++	23810
	+		+	++	++	23810
GPG valeric acid	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 μM	-		-	-	(+)	284
	-		-	-	(+)	217
1 μM	-		-	-	+	2810
	-		-	-	+	1840
0.5 μM	-		-	+	++	2578
	-		-	+	++	3140
0.1μM	-		-	+	++	3507
	-		-	+	++	3670
0.05μM	-		(+)	++	++	11810
	-		(+)	++	++	15879
0.01μM	(+)		+	++	++	23810
	(+)		+	++	++	23810
0.005μM	(+)		+	++	++	23810
	(+)		+	++	++	23810

Table 8 (continued)

GPGR (SEQ ID NO: 1)	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 μ M	-		-	+	++	2840
	-		-	+	++	7810
1 μ M	-		-	+	++	9870
	-		-	+	++	13890
0.5 μ M	-		(+)	++	++	9810
	-		(+)	++	++	15856
0.1 μ M	-		(+)	++	++	21810
	-		(+)	++	++	23870
0.05 μ M	-		+	++	++	23810
	-		+	++	++	23810
0.01 μ M	-		+	++	++	23810
	-		+	++	++	23810
0.005 μ M	-		+	++	++/T	23810
	-		+	++	++/T	23810
GPGR (SEQ ID NO: 1) valeric acid	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 μ M	-		-	(+)	+	3810
	-		-	(+)	+	3810
1 μ M	-		-	+	++	2840
	-		-	+	++	3810
0.5 μ M	-		-	+	++	7810
	-		-	+	++	3840
0.1 μ M	-		(+)	++	++	17890
	-		(+)	++	++	23810
0.05 μ M	-		(+)	++	++	23810
	-		(+)	++	++	23810
0.01 μ M	(+)		+	++	++	23810
	(+)		+	++	++	23810
0.005 μ M	(+)		+	++	++	23810
	(+)		+	++	++	23810
GPGRA (SEQ ID NO: 11)	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 μ M	-		-	-	+	2726
	-		-	-	+	2070
1 μ M	-		-	+	++	3070
	-		-	+	++	2403
0.5 μ M	-		-	++	++	2070
	-		-	++	++	5420
0.1 μ M	-		(+)	++	++	13840
	-		(+)	++	++	9310
0.05 μ M	-		(+)	++	++	13010
	-		(+)	++	++	10910
0.01 μ M	(+)		+	++	++	15650
	(+)		+	++	++	16810
0.005 μ M	(+)		+	++	++	23810
	(+)		+	++	++	23810
GPGRA (SEQ ID NO: 11) valeric acid	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 μ M	-		-	-	-	32
	-		-	-	(+)	108

1 μ M	-		-	-	+	2000
	-		-	-	+	2403
0.5 μ M	-		-	+	++	3810
	-		-	+	++	7810
0.1 μ M	-		(+)	++	++	5600
	-		(+)	++	++	6400
0.05 μ M	-		(+)	++	++	3810
	-		(+)	++	++	11789
0.01 μ M	-		+	++	++	13810
	-		+	++	++	18710
0.005 μ M	(+)		+	++	++	23810
	(+)		+	++	++	23810

SPC3 (SEQ ID NO: 4) monomer valeric acid	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 μ M	-		-	-	-	123
	-		-	-	-	345
1 μ M	-		-	-	(+)	1325
	-		-	-	(+)	4345
0.5 μ M	-		-	+	++	11840
	-		-	+	++	12240
0.1 μ M	-		+	++	++	11810
	-		+	++	++	15307
0.05 μ M	-		+	++	++	23810
	-		+	++	++	21810
0.01 μ M	-		+	++	++ /T	21810
	-		+	++	++/T	21810
0.005 μ M	-		+	++	++ /T	23810
	-		+	++	++/T	23810
SPC3	Day 4	P 24 (pg/ml)	Day 5	Day 6	Day 7	P 24 (pg/ml)
5 μ M	-		-	-	-	12
	-		-	-	-	240
1 μ M	-		-	-	(+)	1692
	-		-	-	(+)	3776
0.5 μ M	-		-	+	++	15173
	-		-	+	++	12840
0.1 μ M	-		(+)	+	++	18810
	-		(+)	++	++	20850
0.05 μ M	-		+	++	++ /T	23810
	-		+	++	++/T	23810
0.01 μ M	-		+	++	++ /T	23810
	-		+	++	++/T	23810
0.005 μ M	-		+	++	++ /T	23810
	-		+	++	++/T	23810

T Cell	-		-	-	-	
	-		-	-	-	
L4-3 1/1000	(+)		++	++	++ /T	19657
	(+)		++	++	++/T	23810

Please replace Table 9, found at page 19 of the substitute specification filed on November 16, 2005 with the following replacement table:

Table 9

Antiviral Activity Experiment on C8166 cells with HIV-1 subtype B NL 4-3

Name	Formula	IC ₅₀ (μM)	IC ₁₀₀ (μM)
GPG	GPG	0.01 0.01	5 5
GPG valeric acid	GPG-NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.01 0.01	0.5 1
GPGR (SEQ ID NO: 1)	GPGR (SEQ ID NO: 1)	0.06 0.1	5 >5
GPGR (SEQ ID NO: 1) valeric acid	GPGR (SEQ ID NO: 1)- NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.03 0.01	5 1
GPGRA (SEQ ID NO: 11)	GPGRA (SEQ ID NO: 11)	0.03 0.02	0.5 >5
GPGRA (SEQ ID NO: 11) valeric acid	GPGRA (SEQ ID NO: 11)- NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.01 0.01	0.1 1
SPC3 monomer valeric acid	GPGRAF (SEQ ID NO: 4)- NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.05	5
SPC3	(GPGRAF (SEQ ID NO: 4)) ₈ -K ₄ -K ₂ -K- NHCH ₂ CH ₂ COOH (SEQ ID NO: 5)	0.5	5

Please replace Table 10, found at page 19 of the substitute specification filed on November 16, 2005 with the following replacement table:

Table 10

Antiviral Activity Experiment on C8166 cells with HIV 1 NDK

Name	Formula	IC ₅₀ (μ M)	IC ₁₀₀ (μ M)
GPG	GPG	0.5	>5
GPG valeric acid	GPG-NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.02	5
GPGR (SEQ ID NO: 1)	GPGR (SEQ ID NO: 1)	0.5	>5
GPGR (SEQ ID NO: 1) valeric acid	GPGR (SEQ ID NO: 1) - NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.3	>5
GPGRA (SEQ ID NO: 11)	GPGRA (SEQ ID NO: 11)	0.04	>5
GPGRA (SEQ ID NO: 11) valeric acid	GPGRA (SEQ ID NO: 11) - NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	>5	5
SPC3 monomer valeric acid	GPGRAF (SEQ ID NO: 4) - NHCH ₂ CH ₂ CH ₂ CH ₂ COOH	0.2	5
SPC3	(GPGRAF (SEQ ID NO: 4)) ₈ -K ₄ -K ₂ -K- NHCH ₂ CH ₂ COOH (SEQ ID NO: 5)	0.6	5